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14. ABSTRACT

Polyacetals are a readily degradable class of polymers with potential uses in the preparation of porous materials and patterned surfaces and in a range of applications as surfactants and drug delivery agents. There are very few synthetic routes to polyacetals that have been reported in the literature to date, which has limited the investigation of these materials. Recently developed organocatalysis systems have been investigated to determine their suitability for the polymerization of model polyacetals based on ethyl glyoxylate, a monomer which can be produced from renewable resources. The preliminary efforts carried out under this STIR grant suggest that organocatalysis can be

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Report Title

Final Report: Degradable Polymers and Block Copolymers from Electron-deficient Carbonyl Compounds (STIR) (7.3 Polymer Chemistry - Synthesis: Architecture and Composition)

ABSTRACT

Polyacetals are a readily degradable class of polymers with potential uses in the preparation of porous materials and patterned surfaces and in a range of applications as surfactants and drug delivery agents. There are very few synthetic routes to polyacetals that have been reported in the literature to date, which has limited the investigation of these materials. Recently developed organocatalysis systems have been investigated to determine their suitability for the polymerization of model polyacetals based on ethyl glyoxylate, a monomer which can be produced from renewable resources. The preliminary efforts carried out under this STIR grant suggest that organocatalysis can be used to control the polymerization of acetals for preparation of degradable polymers suitable for the preparation of porous and lightweight polymer materials.

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Sub Contractors (DD882)

Inventions (DD882)

Scientific Progress

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Technology Transfer

Degradable Polymers and Block Copolymers from Electron-deficient Carbonyl Compounds (STIR)

Robert B. Grubbs, Department of Chemistry, Stony Brook University

List of Appendixes, Illustrations and Tables

Appendices:

Appendix A: Experimental details and polymerization results

Illustrations:

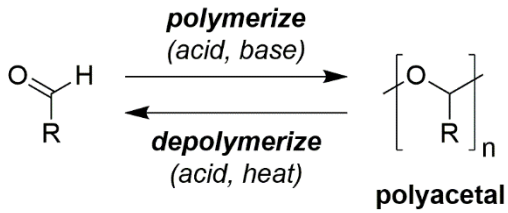
Scheme 1. Polymerization of aldehydes and depolymerization of polyacetals.

Scheme 2. Optimized methods for polymerization of ethyl glyoxylate with DBU

Statement of the problem studied

Polyacetals are a readily degradable class of polymers with potential uses in the preparation of porous materials and patterned surfaces and in a range of applications as surfactants and drug delivery agents (Scheme 1).[1-8] There are very few synthetic routes to polyacetals that have been reported in the literature to date, which has limited the investigation of these materials.[9-15] Recently developed organocatalysis systems have been investigated to determine their suitability for the polymerization of model polyacetals based on ethyl glyoxylate, a monomer which can be produced from renewable resources.

Scheme 1.



ethyl glyoxylate: R = -CO_2Et

Summary of the most important results

Initial efforts at anionic polymerization of glyoxylate salts in water or DMSO were complicated by side reactions of the glyoxylate salts and the difficulty in converting the glyoxylate hydrate to the more reactive glyoxylate in high yield. Given these difficulties, initial efforts were focused on the polymerization of the ethyl glyoxylate, which is soluble in organic solvents and can be more easily dehydrated.

Purification of ethyl glyoxylate, which includes dehydration and deoligomerization of linear and cyclic oligomers, requires considerable effort. Conversion of the hydrate (and glyoxylate oligomers) to the pure aldehyde monomer requires several distillations and transfer of the monomer at reflux directly to the polymerization vessel. Low temperature polymerization (-20 °C) is required to minimize competitive depolymerization, though the effect of temperature on organocatalytic polymerization is still under investigation. Dichloromethane was used as a suitable solvent with a melting point below the polymerization temperature.

To date, direct anionic (with sodium ethoxide) and organocatalytic polymerization, with triethylamine, DBU, and DMAP, of ethyl glyoxylate has been attempted. Polymerization with DBU as the catalyst has proven most effective to date. In order to demonstrate polymerization from alcohol initiators and the potential applicability of these methods to the preparation of block copolymers, the focus has been on the use of an alcohol with an initiating end group that is readily identifiable and quantifiable by ^{1}H NMR. *p*-

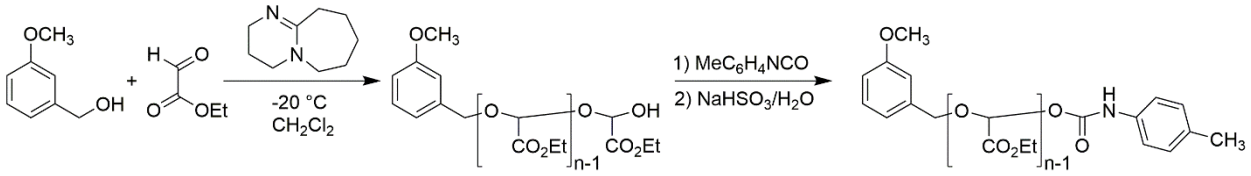
Methoxybenzyl alcohol was used initially, but was replaced with the non-crystalline *m*-methoxybenzyl alcohol for ease of handling.

Covalent chain end-capping groups are necessary to prevent depolymerization of poly(ethyl glyoxylate) at room temperature. Initial attempts to use methyl iodide appeared to be unsuccessful, as evidenced by an apparent drop in molecular weight of the resulting polymers over time at room temperature. Isocyanates have previously been demonstrated to be effective at end-capping the hemiacetal end groups of polyacetals. *p*-Tolyl isocyanate was used to provide a terminal group with a ^{1}H NMR resonance that did not overlap with polymer peaks or the methoxy protons of the initiating alcohol, so that independent quantification of both end groups could be carried out by ^{1}H NMR.

Removal of residual monomer by precipitation of the crude polymer into suitable non-solvents (methanol, hexanes, petroleum ether) proved difficult. Removing residual monomer as the toluene-ethyl glyoxylate azeotrope was also difficult. As an alternative approach, aqueous sodium bisulfite could be added to the polymerization mixture to convert residual monomer to the water-soluble bisulfite complex, which could then be separated. This treatment also appears to be effective in removing DBU and excess isocyanate.

To date, these polymerization efforts have produced polymers of moderate molecular weights (M_n up to 1500 g/mol; $Đ$ 1.4-1.6). Increasing monomer purity and optimizing end-capping conditions have allowed M_n to be increased from preliminary efforts, where M_n values below 1000 g/mol were typically observed. Detailed experimental conditions and tables of results are included in Appendix A.

Scheme 2.



These results suggest that continued optimization of polymerization conditions should allow the controlled organocatalytic chain polymerization of ethyl glyoxylate and other reactive aldehydes, which will enable the preparation of degradable block copolymers and other polymer-based materials through these newly developed polymerization methods.

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Appendix A: Experimental Details and Results

General details

Safety. The minimum personal protective equipment (PPE) required to enter Room 754 is safety glasses with side shields, (100% cotton) lab coat, long pants, and fully enclosed shoes. Reagents are to be handled while wearing nitrile gloves, and if they were flammable or hazardous materials that pose an airborne or explosive hazard, they are to be handled only within a fume hood. All glassware is to be inspected for damage before use. The capacity of reaction flasks should be two to three times the total combined volumes of the reagents and solvents. Chemical exposure is controlled by using minimal amounts of chemicals where possible, manipulating chemicals in contained apparatus in the fume hood or glove box, and wearing appropriate PPE.

Heating of reactions is carried out on temperature-controlled stirrer/hot plates. Nitrogen-filled balloons are used to keep reactions under inert atmosphere. Cold baths are prepared by using sodium chloride/ice in a Dewar flask. The Schlenk line (vacuum gas manifold) is used to provide inert atmosphere during distillation. Prior to use, it is purged with nitrogen for 15-20 mins before being connected to the distillation apparatus. All reactions are carried out in oven-dried glassware.

Materials. Glyoxylic acid monohydrate, sodium pyruvate, ethyl glyoxylate in toluene solution (50% w/w), sodium methoxide deuterated choloform and methyl iodide were obtained from Alfa Aesar. Dimethyl formamide (DMF), dimethyl sulfoxide (DMSO) and methylene chloride (CH_2Cl_2) were obtained from BDH Chemicals. Sodium hydroxide (NaOH) was obtained from Ward's Science. Triethylamine (NEt_3) and calcium chloride were obtained from J.T. Barker. Methanol and ethanol were obtained from Pharmco-AAPER. Disodium malonate and 1,8-Diazabicyclo[5.4.0]undec-7-ene (DBU) were obtained from Acros Organics.

1. Aqueous anionic polymerization of sodium glyoxylate

1.1. Preparation of sodium glyoxylate monohydrate

Glyoxylic acid monohydrate (2.49 g) was dissolved in distilled water (4 ml). NaOH (1.1 g) was dissolved in distilled water (5 ml). NaOH solution was added dropwise to the glyoxylic acid solution until a pH of 8-11 was reached. The neutralized solution was frozen in liquid nitrogen and lyophilized for 48 hrs. ^{1}H NMR [300 MHz, D_2O: δ 9.33 (s, 1H), 5.01 (s, 1H)], [DMSO-d_6: δ 9.37 (s, 1H), 4.62 (s, 1H). Spectral data were consistent with published values[19].

- Glyoxylic acid monohydrate: can cause allergic skin reaction. Also causes serious eye damage
- Sodium hydroxide: causes serve skin burns and eye damage
- Liquid nitrogen: contact with liquid nitrogen causes frostbite and cryogenic burns

1.2. Polymerization of sodium glyoxylate, using disodium malonate as the initiator

Disodium malonate (0.15 g, 1.01 mmol, 1 equiv) and sodium glyoxylate (0.23 g, 2.14 mmol, 1.5 equiv) were dissolved, respectively, in D_2O (1.3 ml). NaOH (0.081 g, 2.03 mmol, 2 equiv) was then added to the reaction mixture. Reaction time was ~5 mins. ^{1}H NMR [300 MHz, D_2O: δ 4.98 (s, 1H), 3.75 (s)]

- Disodium malonate: maybe harmful if inhaled, swallowed or absorbed through the skin. May also cause eye irritation

1.3 Polymerization of sodium glyoxylate with sodium methoxide in D_2O

NaOMe (5.3 mg) was dissolved in D_2O (1 ml) to prepare a stock solution (1 M).

NaGx (100 mg, 0.88 mmol, 50 equiv) was dissolved in D_2O (1 ml). 1M NaOMe in D_2O (0.18 ml, 17.7 μmol, 1 equiv) was added to NaGx solution. The reaction mixture was then placed in a cold bath at 5 °C for 5 hrs. ^{1}H NMR [300 MHz, D_2O: δ 5.04 (s, 1H), 3.90 (s)].

2. Anionic polymerization in sodium glyoxylate in DMSO

2.1. Polymerization of sodium glyoxylate, using sodium methoxide as the initiator

NaOMe (21.8 mg) was added to DMSO (4.36 ml) to prepare a 5 M solution. Solution was sonicated for 15 mins and placed on a shaker until a homogenous orange/brown solution was observed.

Sodium glyoxylate (NaGx) (0.130 g, 1.14 mmol, 12.5 equiv) was dissolved in DMSO (2 ml) after heating at 100 °C for 20 mins. The solution was allowed to cool to room temperature. The solution of NaOMe in DMSO-d_6 (1 ml, 92.5 µmol, 1 equiv) was added to the solution. The reaction vessel was then connected Schlenk line and the reaction was carried out for 140 mins under nitrogen. Two layers were observed. The top layer was decanted off and the bottom layer discarded

Diethyl ether (~10 ml) was added to the top layer of the of reaction mixture. A precipitate was observed. The reaction mixture with precipitate was vacuum filtered. Precipitate was air dried for 36 hrs. ^{1}H NMR [300 MHz, D_2O: δ 8.39 (s), 4.99 (s, 1H), 3.88 (s), 2.66 (s)].

- Sodium methoxide: causes severe skin burns and eye damage. Also harmful if swallowed. Caution was taken to prevent the inhalation of dust or mist and skin was washed thoroughly after handling
- DMSO: combustible liquid. Caution was taken to keep away from heat/sparks and hot surfaces
- Diethyl ether: extremely flammable liquid and vapor. Causes serious eye irritation and may cause drowsiness or dizziness. Caution was taken to keep away from heat/sparks and hot surfaces.

2.2. Polymerization of sodium glyoxylate in DMSO-d_6 using sodium methoxide as the initiator

NaOMe (3.5 mg) was added to DMSO-d_6 (2.8 ml) and the resulting solution was then sonicated for 15 mins.

NaGx (5.3 mg, 46.3 µmol, 25 equiv) was mixed with DMSO-d_6 (1 ml) and heated at 100 °C for 20 mins to complete dissolution. Activated molecular sieves (4Å) were added to the hot solution and the solution was then allowed to cool to room temperature. The solution of NaOMe in DMSO-d_6 (80 µL, 1.85 µmol 1 equiv) was added to the solution. The reaction vessel was heated at 30 °C for 30 mins. ^{1}H NMR [300 MHz, D_2O: δ 9.36 (s, 1H), 8.50 (s), 3.37 (s)].

Exp #8 - #10 followed a similar procedure, while the desired temperatures were obtained using an oil bath. Exp# 9 and #10 used sodium pyruvate as the monomer, instead of sodium glyoxylate.

2.3. Polymerization of sodium glyoxylate with sodium methoxide and molecular sieves

NaOMe (2.6 mg) was added to DMSO-d_6 (2.0 ml). Solution was then sonicated for 15 mins.

NaGx (8.3 mg, 70 µmol, 25 equiv) was mixed with DMSO-d_6 (1 ml) and heated at 100 °C for 20 mins to complete dissolution. Activated molecular sieves (4Å) were added to the hot solution and the solution was allowed to cool to room temperature. The solution of NaOMe in DMSO-d_6 (0.12 ml, 2.9 µmol, 1 equiv) was added to the reaction solution. The reaction vessel was cooled to 20 °C for 5 hrs. ^{1}H NMR [300 MHz, D_2O: δ 9.36 (s, 1H), 3.35 (s)].

3. Polymerization of ethyl glyoxylate

3.1. Triethylamine-catalyzed polymerization of ethyl glyoxylate (1)

Ethyl glyoxylate in toluene solution (20 mL) was fractionally distilled under vacuum (55 ºC, 125 mbar) over P_2O_5 to remove toluene and trace water in the first, discarded fraction. The residue was then distilled twice successively over P_2O_5 at atmospheric pressure under nitrogen protection at 130 ºC to obtain the purified monomer. This pale yellow liquid (2.5 mL, 25 mmol, 2000 equiv.) was dissolved in dichloromethane (2.5 mL) and NEt_3 (1.75 µL, 12.5 µmol, 1 equiv.). The solution was stirred for one hour

at -20 ºC. Purification by precipitation was attempted in methanol, hexanes and petroleum ether. ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.48-5.75 (m), 4.12-4.38 (m), 1.24-1.44 (m).

- Ethyl glyoxylate in toluene: highly flammable liquid and vapor. Maybe fatal if swallowed and enters airways. Causes skin irritation. May cause allergic skin reaction, drowsiness or dizziness. Suspected of damaging fertility or the unborn child. May cause damage to organs through prolonged or repeated exposure. Caution was taken to keep away from heat/ sparks/ hot surfaces, and to prevent the inhalation of dust/ gas/ mist/ vapors or spray. Skin was also washed thoroughly after use.
- NEt_3: highly flammable liquid and vapor. Harmful if swallowed. Toxic in contact with skin or if inhaled. Causes severe skin burns and eye damage. May cause respiratory irritation. Caution was taken to keep away from heat/ sparks and hot surfaces, and to prevent the inhalation of dust/ fume/ gas/ mist/ vapors and spray. Container was kept tightly closed
- P_2O_5: fatal is inhaled. Causes severe skin burns and eye damage. Caution was taken to prevent the inhalation of dust/ fume/ gas/ vapors/ spray. Skin was also washed thoroughly after use
- Dichloromethane: Causes skin and eye irritation. May cause respiratory irritation, drowsiness or dizziness. Suspected of causing cancer. May cause damage to organs (liver and blood) through prolonged or repeated exposure if swallowed. May also cause damage to organs (Central nervous system) through prolonged or repeated exposure in inhaled.
- Methanol: highly flammable liquid and vapor. Toxic if swallowed, in contact with skin or if inhaled. Also causes damage to organs. Caution was taken to keep away from heat/ sparks and hot surfaces, and to prevent the inhalation of dust/ fume/ gas/ mist/ vapors and spray.
- Hexanes and petroleum ether: highly flammable liquid and vapor. Maybe fatal if swallowed and enters airways. May cause drowsiness or dizziness. Suspected of damaging fertility of he unborn child. Caution was taken to keep away from heat/ sparks and hot surfaces, and to prevent the inhalation of dust/ fume/ gas/ mist/ vapors and spray.

3.2. Control polymerization of ethyl glyoxylate with ethanol (2 and 3)

The same distillation and polymerization procedure was conducted to obtain PEtG as describe above. However, toluene was distilled between 25 and 55 °C. EtG was doubly distilled at 50 °C under nitrogen protection. Ethyl glyoxylate was then refluxed for 30 mins under nitrogen protection. A yellow solution was obtained. In polymerization #2, instead of NEt_3, ethanol (0.73 µL, 12.5 µmol, 1 equiv) was used.

- Ethanol: highly flammable liquid and vapor. Caution was taken to keep away from heat/ sparks and hot surfaces, and to prevent the inhalation of dust/ fume/ gas/ mist/ vapors and spray. Container was kept tightly closed

3.4. Control polymerization of ethyl glyoxylate in DMF with no added initiator or catalyst (4)

The same distillation and polymerization procedure was conducted as describe in the general procedure. However, the second distillation temperature of EtG was 88 °C. No external initiator was used. The solvent used in polymerization #4 was DMF in volume equivalent to EtG.

- Dimethyl Formamide (DMF): flammable liquid and vapor. Harmful in contact with skin or if inhaled. Causes serious eye irritation. Suspected of damaging fertility of he unborn child. Caution was taken to keep away from heat/ sparks and hot surfaces, and to prevent the inhalation of dust/ fume /gas/ mist/ vapors and spray. Container was kept tightly closed

3.5. Polymerization of ethyl glyoxylate with DBU or trimethylamine and methyl iodide capping (5 and 6)

The same distillation and polymerization procedure as described in the general procedure. However, ethanol and CH_2Cl_2 were dried over activated molecular sieves (3 Å), while NEt_3 and DBU were dried over alumina. For polymerization #5, the monomer (EtG, 2.5 ml, 25 mmol, 1000 equiv) was dissolved in

CH_2Cl_2 (2.5 ml), DBU (3.7 µL, 0.25 mmol, 1 equiv) and ethanol (1.4 µL, 0.25 mmol, 1 equiv). For polymerization #6, instead of DBU, NEt_3 (35 µL, 0.25 mmol, 1 equiv) was used. After both polymerizations, methyl iodide (7.8 µL, 1.25 mmol, 5 equiv) was added to end-cap polymers

- DBU: May be corrosive to metals. Toxic if swallowed. Causes severe skin burns and eye damage. Skin was washed thoroughly after handling.
- Alumina: Harmful if inhaled. Caution was taken to avoid breathing dust/ fume/ gas/ mist/ vapors or sprays

3.6. Polymerization of ethyl glyoxylate with DBU and MeI end-capping (7 and 8)

The same distillation and polymerization as described in the general procedure. However, EtG was triply distilled. The same reagent and equivalents were used as in polymerization #5. The polymerization lasted 5 hrs at -20 °C. Methyl iodide (7.8 µL, 1.25 mmol, 5 equiv) was used to end-cap polymerization #7; methyl iodide (23.4 µL, 3.75 mmol, 15 equiv) was used to end-cap polymerization #8. The solution was then stirred at room temperature for 18 hrs and a further 14 hrs at 40 °C.

- Methyl iodide: toxic if swallowed or in contact with skin. Causes skin irritation. May cause an allergic skin reaction. Causes serious eye damage. Fatal if inhaled. May cause respiratory irritation. Suspected of causing cancer. Caution was taken to avoid breathing dust/ fume/ gas/ mist/ vapors or sprays. Chemical was handled in fume hood.

3.7. Polymerization of ethyl glyoxylate with DBU and cold MeI end-capping (9)

The same distillation and polymerization as described in polymerization #5. However, EtG was triply distilled. EtG (5 ml, 50 mmol, 500 equiv) was dissolved in CH_2Cl_2 (5 ml), ethanol (6 µL, 1.0 mmol, 1 equiv) and DBU (14.8 µL, 1.0 mmol, 1 equiv). The polymerization lasted for 2 hrs at -20 °C. Methyl iodide (15.6 µL, 2.5 mmol, 2.5 equiv) was added to end-cap the polymer at -20 °C and allowed to gradually increase in temperature up to -10 °C.

3.8. Polymerization of ethyl glyoxylate with DBU/ethanol – comparison of MeI and PhNCO end-capping (10 and 11)

The same distillation and polymerization as described in polymerization #5. EtG (2.5 ml, 25 mmol, 250 equiv) was dissolved in CH_2Cl_2 (2.5 ml), ethanol (6 µL, 1.0 mmol, 1 equiv) and DBU (14.8 µL, 1.0 mmol, 1 equiv). The polymerization lasted for 2 hrs at -20 °C. Methyl iodide (15.6 µL, 2.5 mmol, 2.5 equiv) was added to end-cap the polymer at -20 °C and allowed to gradually increase in temperature up to -10 °C (polymerization #10), while Phenyl isocyanate (460 µL, 4.2 mmol, 4.2 equiv) was used as an end-cap in polymerization #11.

3.9. Polymerization of ethyl glyoxylate with DBU/ethanol and PhNCO end-capping (12)

The same distillation and polymerization as described in polymerization #5. EtG was triply distilled. EtG (3.0 ml, 30 mmol, 1000 equiv) was dissolved in CH_2Cl_2 (3 ml), ethanol (1.8 µL, 0.3 mmol, 1 equiv) and DBU (4.4 µL, 0.3 mmol, 1 equiv). The polymerization lasted for 2 hrs at -20 °C. Phenyl isocyanate (492.8 µL, 4.5 mmol, 15 equiv) was used to end-cap

3.10 Polymerization of with distilled/refluxed ethyl glyoxylate with DBU/4-methoxybenzyl alcohol with tolyl isocyanate end-capping (16):

Monomer purification. Ethyl glyoxylate (EtG) in toluene solution (24 mL, 50% w/w) was fractionally distilled under vacuum (55°C, 125 mbar) over phosphorus pentoxide (P_2O_5) to remove toluene and trace water in the first, discarded fraction. The residue was then fractionally distilled (128-135 °C) over P_2O_5 at atmospheric pressure under nitrogen protection at 130 °C to obtain the purified EtG. Using a syringe purged with nitrogen, distilled EtG was transferred to a rbf containing P_2O_5 and stored under nitrogen. EtG was then fractionally distilled a second time. This process was repeated a third time. Both the second and the third distilling temperatures were the same as the first distillation. Using nitrogen-purged syringe,

the triply distilled EtG was transferred to a double necked rbf and refluxed for ~2 hrs. The refluxing was performed to prevent the formation of oligomers, which has been observed to a higher degree if EtG is not kept at high temperatures.

Polymerization. A 20 mL scintillation vial, sealed with a septum, was kept under nitrogen using a nitrogen filled balloon. To the scintillation vial, methylene chloride (CH_2Cl_2) was added (1.5 mL) and placed into cold bath, with the cryocool set at -20 °C but the actual temperature was between 5-10 °C (Nb: only after polymerization # 19, a thermometer was used to adjust the cryocool unit to -20 °C). Using a nitrogen-purged syringe, EtG (1.5 mL, 15 mmol) heated at reflux was transferred to the scintillation vial. DBU (44.8 μL, 0.3 mmol) was added, followed by 4-methoxybenzyl alcohol (36.7 μL, 0.3 mmol). After 1 hr, the scintillation vial was removed from the cold bath. Tolyl isocyanate (0.19 mL, 1.5 mmol) was added to the reaction vial ~15 mins after removed from cold bath (approximately at room temperature). The vial was then allowed to stand for 22 hrs at room temperature under nitrogen. It was then heated at 40 °C for 16 hrs. These post polymerization steps were done as outlined by Burel and company, who first polymerized EtG.

Polymer isolation. Methanol (10 mL) was added to the reaction vial and stirred until polymerization mixture was dissolved. Aqueous sodium bisulfite (5 mL, 1.5 mmol, 0.3 mol/L) was then added and precipitation was observed. The precipitate was filtered through glass wool in a Pasteur pipette. Both the isolated polymer (a viscous liquid) and filtrate were collected. The filtrate was then evaporated to dryness on a rotovap and a vicious liquid was collected and vacuum dried along with the isolated polymer at 25 °C for ~46 hrs. Samples of the residue and filtrate were prepared for ^{1}H NMR analysis using deuterated chloroform ($CDCl_3$) as the solvent. A sample of both the isolated polymer and filtrate were prepared for SEC by making a 1.0 mg/ml solution in THF.

3.11. Polymerization of distilled/refluxed ethyl glyoxylate with DMAP/4-methoxybenzyl alcohol and tolyl isocyanate end-capping (17):

The EtG used for this polymerization was acquired from the EtG solution in toluene from the purification step in polymerization #16. A 20 mL scintillation vial, sealed with a septum, was kept under nitrogen using a nitrogen filled balloon. To the scintillation vial, methylene chloride (CH_2Cl_2) was added (1.5 mL) and placed into cold bath, with the cyocool set at -20 °C but the actual temperature was between 5-10 °C. Using a nitrogen-purged syringe, EtG (1.5 mL, 15 mmol) heated at reflux was transferred to the scintillation vial DMAP (0.19 mL, 2.0 mmol/mL in CH_2Cl_2) was added, followed by 4-methoxybenzyl alcohol (36.7 μL, 0.3 mmol). After 1 hr, the scintillation vial was removed from the cold bath. Tolyl isocyanate (0.19 mL, 1.5 mmol) was added to the reaction vial ~15 mins after removed from cold bath (approximately at room temperature). The vial was then allowed to stand for 22 hrs at room temperature under nitrogen. It was then heated at 40 °C for 16 hrs. The isolation steps were the same to those of polymerization #16

3.12. Polymerization of refluxed/distilled ethyl glyoxylate with DBU/4-methoxybenzyl alcohol or DMAP/4-methoxybenzyl alcohol with tolyl isocyanate end-capping (20, 21):

The same purification and polymerization steps were used as in polymerization #16. A 20 mL scintillation vial, sealed with a septum, was kept under nitrogen using a nitrogen filled balloon. To the scintillation vial, methylene chloride (CH_2Cl_2) was added (3 mL) and placed into cold bath, with the cryocool set at -20 °C. Using a nitrogen-purged syringe, EtG (2.5 mL, 25 mmol, 100 equiv) heated at reflux was transferred to the scintillation vial. DBU (37.3 μL, 0.25 mmol, 1 equiv) was added in polymerization #18, while DMAP (0.125 mL, 2.0 mmol/mL in CH_2Cl_2, 1 equiv) was added in polymerization #19, followed by 4-methoxybenzyl alcohol (30.6 μL, 0.25 mmol, 1equiv). After 1 hr, the scintillation vial was removed from the cold bath. Tolyl isocyanate (0.19 mL, 1.5 mmol, 6 equiv) was added to the reaction vial ~15 mins after removed from cold bath (approximately at room temperature). The vial was then allowed to stand for 22 hrs at room temperature under nitrogen. It was then heated at 40 °C for 16 hrs. The isolation steps were similar to those of polymerization #16

3.13. Polymerizations and control polymerizations with aqueous sodium bisulfite work-up (26-33)

Monomer Purification. Ethyl glyoxylate (EtG) in toluene solution (48 mL, 50% w/w) was fractionally distilled under vacuum (55°C, 125 mbar) over phosphorus pentoxide (P_2O_5) to remove toluene and trace water in the first, discarded fraction. The residue was then fractionally distilled (128-135 °C) over P_2O_5 at atmospheric pressure under nitrogen protection at 130 °C to obtain the purified EtG. Using a syringe purged with nitrogen, distilled EtG was transferred to a rbf containing P_2O_5 and stored under nitrogen. EtG was then fractionally distilled a second time. This process was repeated a third time. Both the second and the third distilling temperatures were the same as the first distillation. Using nitrogen-purged syringe, the triply distilled EtG was transferred to a double necked rbf and refluxed for ~2 hrs. The refluxing was performed to prevent the formation of oligomers, which has been observed to a higher degree if EtG is not kept at high temperatures

Polymer isolation. Aqueous sodium bisulfite (5 mL, 1.5 mmol, 0.3 mol/L) was then added and precipitation was observed. The precipitate was filtered through glass wool in a Pasteur pipette. Both the isolated polymer (a viscous liquid) and filtrate were collected. The isolated polymer was vacuum dried at 25 °C for ~46 hrs. Samples of the isolated polymer were prepared for ^{1}H NMR analysis using deuterated chloroform ($CDCl_3$) as the solvent. A sample of the isolated polymer was prepared for SEC by making a 1.0 mg/ml solution in THF

3.13.1. Polymerization #26 (without Initiator or end-cap)

A 20 mL scintillation vial, sealed with a septum, was nitrogen-purged and kept under nitrogen using a nitrogen filled balloon. To the scintillation vial, methylene chloride (CH_2Cl_2) was added (3.0 mL) followed by DBU (44.8 µL, 0.3 mmol) and placed into cold bath, with the cyocool set at -20 °C, using a cryocool controller and a thermometer. Using a nitrogen-purged syringe, EtG (3.0 mL, 30 mmol) heated at reflux was transferred to the scintillation vial. After 3 hrs, the scintillation vial was removed from the cold bath. The vial was then allowed to stand for ~22 hrs at room temperature under nitrogen. It was then heated at 40 °C for ~16 hrs. These post polymerization steps were done as outlined by Burel and company, who first polymerized EtG.

3.13.2. Polymerization #27 (without initiator)

A 20 mL scintillation vial, sealed with a septum, was nitrogen-purged and kept under nitrogen using a nitrogen filled balloon. To the scintillation vial, methylene chloride (CH_2Cl_2) was added (3.0 mL) followed by DBU (44.8 µL, 0.3 mmol) and placed into cold bath, with the cyocool set at -20 °C, using a cryocool controller and a thermometer. Using a nitrogen-purged syringe, EtG (3.0 mL, 30 mmol) heated at reflux was transferred to the scintillation vial. After 3 hrs, the scintillation vial was removed from the cold bath. The vial was then allowed to stand for ~22 hrs at room temperature under nitrogen. It was then heated at 40 °C for ~16 hrs. However, Tolyl isocyanate (0.19 mL, 1.5 mmol) was added to end-cap the polymer ~15 mins after the scintillation vial was removed from the cold bath.

3.13.3. Polymerization #28 (without end-cap)

A 20 mL scintillation vial, sealed with a septum, was nitrogen-purged and kept under nitrogen using a nitrogen filled balloon. To the scintillation vial, methylene chloride (CH_2Cl_2) was added (3.0 mL) followed by DBU (44.8 µL, 0.3 mmol), then 4-methoxybenzyl alcohol (4-MeOBnOH) (36.7 µL, 0.3 mmol) and placed into cold bath, with the cyocool set at -20 °C, using a cryocool controller and a thermometer. Using a nitrogen-purged syringe, EtG (3.0 mL, 30 mmol) heated at reflux was transferred to the scintillation vial. After 3 hrs, the scintillation vial was removed from the cold bath. The vial was then allowed to stand for ~22 hrs at room temperature under nitrogen. It was then heated at 40 °C for ~16 hrs.

3.13.4. Polymerization #29

A 20 mL scintillation vial, sealed with a septum, was nitrogen-purged and kept under nitrogen using a nitrogen filled balloon. To the scintillation vial, methylene chloride (CH_2Cl_2) was added (3.0 mL) followed by DBU (44.8 µL, 0.3 mmol), then 4-methoxybenzyl alcohol (4-MeOBnOH) (36.7 µL, 0.3 mmol) and placed into cold bath, with the cryocool set at -20 °C, using a cryocool controller and a thermometer. Using a nitrogen-purged syringe, EtG (3.0 mL, 30 mmol) heated at reflux was transferred to the scintillation vial. After 3 hrs, the scintillation vial was removed from the cold bath. The vial was then allowed to stand for ~22 hrs at room temperature under nitrogen. It was then heated at 40 °C for ~16 hrs. Tolyl isocyanate (0.19 mL, 1.5 mmol) was added to end-cap the polymer ~15 mins after the scintillation vial was removed from the cold bath.

3.14. Polymerization of ethyl glyoxylate with DBU/3-methoxybenzyl alcohol with tolyl isocyanate end-capping (30-33)

3.14.1. 30 minutes (30)

The polymerization steps were similar to polymerization #29. However, instead of using 4-methoxybenzyl alcohol as the initiator, 3-methoxybenzyl alcohol (36.7 µL, 0.3 mmol) was used; this was added along with DBU (44.8 µL, 0.3 mmol) to the scintillation vial containing CH_2Cl_2, prior to the addition of the monomer EtG (3.0 mL, 30 mmol). Tolyl isocyanate (0.19 mL, 1.5 mmol) was added to end-cap the polymer after a polymerization time of ~30 mins. The end-cap was added to the scintillation vial at -20 °C in the cold bath. The scintillation vial was removed ~10 mins after end-cap. End-capping was allowed to proceed overnight.

3.14.2. 60 minutes (31)

The polymerization steps were similar to polymerization #30. 3-methoxybenzyl alcohol (36.7 µL, 0.3 mmol) was used; this was added along with DBU (44.8 µL, 0.3 mmol) to the scintillation vial containing CH_2Cl_2, prior to the addition of the monomer EtG (3.0 mL, 30 mmol). Tolyl isocyanate (0.19 mL, 1.5 mmol) was added to end-cap the polymer after a polymerization time of 1 hr. The end-cap was added to the scintillation vial at -20 °C in the cold bath. The scintillation vial was removed ~10 mins after end-cap. End-capping was allowed to proceed overnight

3.14.3. 90 minutes (32)

The polymerization steps were similar to polymerization #30. 3-methoxybenzyl alcohol (36.7 µL, 0.3 mmol) was used; this was added along with DBU (44.8 µL, 0.3 mmol) to the scintillation vial containing CH_2Cl_2, prior to the addition of the monomer EtG (3.0 mL, 30 mmol). Tolyl isocyanate (0.19 mL, 1.5 mmol) was added to end-cap the polymer after a polymerization time of 1.5 hrs. The end-cap was added to the scintillation vial at -20 °C in the cold bath. The scintillation vial was removed ~10 mins after end-cap. End-capping was allowed to proceed overnight

3.14.4. 120 minutes (33)

The polymerization steps were similar to polymerization #30. 3-methoxybenzyl alcohol (36.7 µL, 0.3 mmol) was used; this was added along with DBU (44.8 µL, 0.3 mmol) to the scintillation vial containing CH_2Cl_2, prior to the addition of the monomer EtG (3.0 mL, 30 mmol). Tolyl isocyanate (0.19 mL, 1.5 mmol) was added to end-cap the polymer after a polymerization time of 2 hrs. The end-cap was added to the scintillation vial at -20 °C in the cold bath. The scintillation vial was removed ~10 mins after end-cap. End-capping was allowed to proceed overnight

Tables of Selected Polymerization Data

Abbreviations used in Tables:
EtG - ethyl glyoxylate
DBU – 1,8-diazabicyclo[5.4.0]undec-7-ene
DMAP – *N*,*N*-dimethylaminopyridine
4MBA – 4-methoxybenzyl alcohol
3MBA – 3-methoxybenzyl alcohol
TIC – tolyl isocyanate

Table 1. Polymerizations of ethyl glyoxylate from ethanol

Run #	EtG (equiv)	EtOH (equiv)	DBU (equiv)	End-cap (equiv)	% Monomer conversion	M_n (g/mol)	Đ
7	100	1	1	5 (MeI)	36.0	176	1.04
8	100	1	1	15 (MeI)	33.4	172	1.03
9	50	1	1	2.5 (MeI)	11.4	642	1.08
10	25	1	1	2.5 (MeI)	38.8	153	1.07
11	25	1	1	4.2 (PhNCO)	54	1756	1.40

Table 2. Polymerizations of ethyl glyoxylate from methoxybenzyl alcohol initiators.

Run #	[EtG]/ [catalyst]	Catalyst	Initiator	TIC (equiv)	t (hrs)	EtG purity (%)	conv (%)	Mn, (g/mol)	
								^{1}H NMR[b]	GPC
16	50	DBU	4MBA	10	1	60	53	1052	939
17	50	DMAP	4MBA	10	1	60	46	956	949
18	100	DBU	4MBA	5	1	25	10	-----	449
19	100	DMAP	4MBA	5	1	25	---	----	344
20	100	DBU	4MBA	6	1	80	45	1376	433
21	100	DMAP	4MBA	6	1	80	34	1106	352
22	100	DBU	4MBA	5	3	80	65	2183	1209
23	100	DMAP	4MBA	5	3	80	54	1762	1546
24	100	DBU	4MBA	6	5	80	65	1578	663
25	100	DMAP	4MBA	6	5	80	50	1549	973
26	100	DBU	-----	-----	3	80	53	-----	
27	100	DBU	-----	5	3	80	62	2262	
28	100	DBU	4MBA	-----	3	80	47	-----	
29	100	DBU	4MBA	5	3	80	59	1658	
30	100	DBU	3MBA	5	0.5	50	17	1596	
31	100	DBU	3MBA	5	1	50	13	1076	
32	100	DBU	3MBA	5	1.5	50	20	1315	
33	100	DBU	3MBA	5	2	50	4	1042	